Prognostic Factors Influencing Survival in Gastrointestinal Leiomyosarcomas

Implications for Surgical Management and Staging

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The appropriate surgical therapeutic options for either localized or more advanced disease in patients with gastrointestinal leiomyosarcomas remain unclear. A staging classification for this disease has not been adopted nor risk factors identifying patients at risk for recurrence defined. To address these issues, this study evaluated the influence of various clinicopathologic variables on overall and disease-free survival. In an univariate analysis of overall survival involving 191 patients, the Cox proportional hazards model identified four factors that were associated with a significantly better outcome: complete resection without tumor rupture ($p < 0.001$), localized lesions ($p < 0.001$), low grade of tumor ($p = 0.02$), and tumors smaller than 5 cm ($p = 0.03$). When interactive effects of these factors were taken into account, however, type of resection of the tumor was selected as the only significant prognostic factor in a multivariate analysis. Complete resection without tumor rupture improved overall survival of patients with localized disease (median, 46 months) as well as those with contiguous organ invasion (median, 36 months) or peritoneal implants (median, 36 months). In contrast, patients with incomplete resections survived for a median of 21 months. Patients with tumor rupture, despite removal of all gross disease, behaved similarly to those with incomplete resections; median survival was only 17 months. For disease-free survival, important determinants selected from a multivariate analysis were tumor rupture ($p = 0.002$), contiguous organ invasion ($p = 0.02$) and high tumor grade ($p = 0.02$). A staging classification incorporating these prognostic factors of significance was evaluated using a TGM system: T1 (<5 cm), T2 (≥5 cm), T3 (contiguous organ invasion or peritoneal implants), T4 (tumor rupture); G: G1 (low grade), G2 (high grade); M: M0 (no metastases), M1 (metastases present). The corresponding 5-year overall survivals for stages I, II, III, IVA, and IVB were 75%, 52%, 28%, 12%, and 7%. Disease-free survival at 2 years after surgery was 89%, 57%, and 47% for stages I, II, and III, respectively. In conclusion, surgery remains the primary modality of treatment for patients with gastrointestinal leiomyosarcomas, and complete resection of all disease without tumor rupture, even of locally advanced disease, improves overall and disease-free survival. A staging classification appears feasible and is recommended to determine outcome in patients with leiomyosarcomas arising from the gastrointestinal tract.

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SURGERY REMAINS THE the primary modality of treatment for patients with gastrointestinal leiomyosarcomas. Therapeutic options for localized or more advanced stages of disease, however, have not been assessed with respect to clinical outcome. For example, the ability of radical extirpative surgery to improve survival of patients with primary tumor invading contiguous organ or associated with peritoneal implants remains in doubt. For localized lesions, unclear issues include the adequate extent of primary organ resection and the need for wide excision of attached mesentery or regional lymphadenectomy. Further, prognostic factors that can identify high-risk groups for recurrence, despite such "curative surgery," have not been elucidated. In contrast to soft tissue tumors arising from other sites,[1] a staging classification has not been adopted for gastrointestinal leiomyosarcomas. In an attempt to address these issues, this study evaluated the influence of various clinicopathologic factors, including type of surgery performed, on overall and disease-free survival. The results of these analyses are used in recommending rational therapeutic strategies for patients with gastrointestinal leiomyosarcomas. Finally, we also examined the feasibility of formulating a staging classification based on significant prognostic factors.

Methods

The records of all patients with gastrointestinal leiomyosarcomas referred to University of Texas M. D. An-

Dr. Ng is a visiting fellow from Singapore and sponsored by the Ministry of Health and Singapore Cancer Society.

Supported by the Del and Denis McCarthy Fund for Surgical Oncology Research and the R.G.K. Foundation Fund for Sarcoma Research.

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Accepted for publication May 30, 1991.

derson Cancer Center (UTMDACC) from January 1957 to December 1987 were reviewed. All tumors with the diagnosis of leiomyosarcoma that originated from the gastrointestinal tract and were confirmed by a UTMDACC pathologist were included in this study. Primary tumors attached to the mesentery or omentum were also included and labeled as arising from an "other" site of origin. Patients with leiomyosarcomas arising from the retroperitoneum or esophagus or patients with other synchronous or metachronous malignancies were excluded. The last recorded date of follow-up was April 15, 1990. The median follow-up of surviving patients was 68 months (range, 15 to 178 months).

Definitions and Criteria

The tumor size used was as determined by the pathologist at the institution where the primary operation was performed. The tumor grade assigned and criteria for such grading was determined by the reviewing pathologist at UTMDACC at the time of patient referral. The type of operation performed was classified as complete resection with or without tumor rupture or incomplete resection. Complete resections were defined as removal of all gross disease at operation; conversely, incomplete resections implied gross residual disease remaining after surgery. Tumor rupture referred to those patients in whom complete resections were performed but the tumor ruptured either at the time of resection (n = 17) or because of perforation just before surgery (n = 7). Disease extent was determined intraoperatively. Localized lesions were confined to the primary organ of origin; contiguous organ involvement had to be confirmed by the histologic presence of primary tumor invasion. Resectable implants were peritoneal deposits within the abdominal cavity, excluding liver, and removable by surgery. Unresectable implants were lesions in similar location but not amenable to surgical removal. Metastases were either deposits in the liver noted at operation or in other extra-abdominal sites detected by appropriate investigations.

Statistical Methods

Survival curves incorporating various prognostic factors for overall and disease-free survival were computed using the methods of Berkson and Gage.[2] Zero time was at initial surgery; the terminal event was either death due to disease or initial recurrence, as appropriate. The Cox proportional hazards model was used in identifying factors of significance.[3] This was performed with effects of individual variables considered individually (univariate analysis) and when the joint effects of variables were modeled by Cox stepwise regression analysis (multivariate analysis). In the analysis of prognostic factors by site of tumor, comparison of survival experiences was performed using the Lee-Desu statistic.[4] P values < 0.05 were considered statistically significant.

Results

Patient Characteristics

During the study period, 201 patients with gastrointestinal leiomyosarcomas were referred to this institution for primary therapy, adjunctive therapy after surgery, or treatment of recurrences. Ten patients with either synchronous or metachronous secondary malignancies were excluded from this study. Secondary malignancies consisted of breast carcinoma (2), colorectal carcinoma (3), lymphoma (3), hepatocellular carcinoma (1), and urethral carcinoma (1). Demographic and clinical features of the patient population are listed in Table 1. After exclusions, 191 patients were included in this study and the median age was 54 years (range, 12 to 85 years). Caucasians were the predominant race (87%) and there was a mild male preponderance (1.4:1). Tumors arising from the stomach (38%) and small bowel (41%) were the most common sites of origin. Most patients were treated with adjuvant systemic chemotherapy (76%); some patients received regional therapy (hepatic arterial infusions or chemoembolization) or radiotherapy for recurrences. The response to these therapies were marginal, and results of chemotherapy administered in a adjuvant setting or for recurrences were not thought to alter the clinical outcome.[5]

Overall Survival

All Patients. **Univariate Analysis.** Actuarial 5-year survival for all patients was 28% (Fig. 1). The median survival

TABLE 1. *Characteristics of Patient Population* (n = 191)

Characteristic	N (%)
Sex	
M	110 (58)
F	81 (42)
Ethnicity	
White	167 (87)
Black	9 (5)
Hispanic	12 (6)
Other	3 (2)
Age	
12–39	32 (17)
40–49	37 (19)
50–59	54 (28)
60–69	42 (22)
≥70	26 (14)
Site of primary lesion	
Stomach	72 (38)
Small bowel	79 (41)
Large bowel	22 (12)
Other	18 (9)
Chemotherapy	
Yes	145 (76)
No	30 (16)
Unknown	16 (8)
Radiation therapy	
Yes	38 (20)
No	130 (68)
Unknown	23 (12)

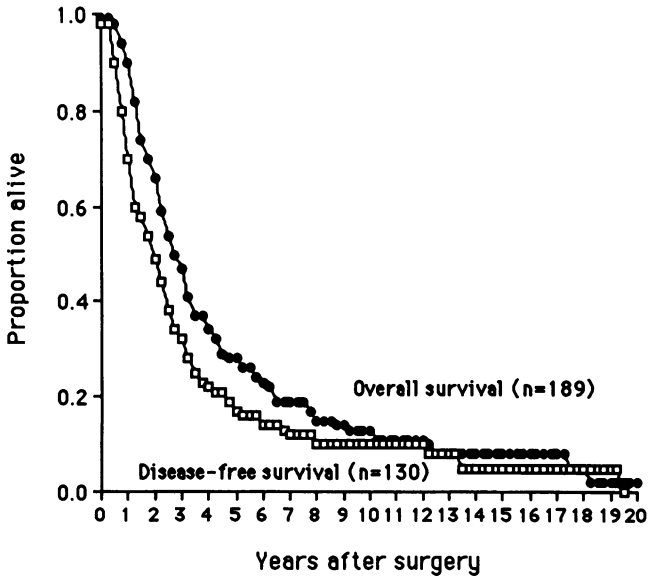

FIG. 1. Overall and disease-free survival rates for entire cohort. Disease-free survival based on patients with complete resection with and without tumor rupture.

time of the entire cohort was 29 months (range, 1 to 284 months). Seven prognostic factors were analyzed: type of operation, extent of disease, tumor grade, and tumor size correlated significantly with overall survivorship (Table 2).

Patients with complete resections showed improvements in overall survival (median, 48 months) compared with incomplete resections (median, 21 months; $p < 0.001$; Fig. 2). Tumor rupture at the time of surgery, despite the removal of all gross disease, was associated with an adverse influence on overall survival (median, 17 months). Progressive extent of disease at the time of surgery showed a stepwise inverse correlation with overall survival (Table 2 and Fig. 3). Localized tumors were associated with a favorable outcome and a median survival of 46 months. In contrast, patients with unresectable peritoneal implants or metastases experienced median survivals of 23 and 19 months, respectively. Tumor grade was also significant in predicting overall survival ($p = 0.018$, Fig. 4). The median survival of patients with low-grade tumors was 41 months, compared with 36 months for those with high-grade tumors. Patients with tumors smaller than 5 cm also experienced prolonged survivals (median, 68 months) when compared with patients with 5- to 10-cm tumors (median, 32 months) or greater than 10 cm (median, 27 months; Fig. 5). Site of origin, age, and sex were not significant prognostic factors (Table 2).

Multivariate Analysis. Only patients with complete information regarding type of operation, extent of disease, tumor grade, and size could be included in a stepwise regression analysis to evaluate the relative importance of various prognostic factors. Because the grade of tumor was not specified in many patients, the sample size would have been significantly reduced if grade was included as a variable to be evaluated. To overcome this limitation, analysis was performed with and without grade of tumor entered into Cox's model. The corresponding sample size was 100 and 149 patients, respectively. From both sets of analysis, type of operation was selected as the only significant prognostic factor. Other factors entered subsequently into the model (extent of disease, tumor grade, and tumor size) did not provide additional information regarding survival. Patients with incomplete resections or tumor rupture had a relative risk for death of 3.4 (95% confidence interval, 2.0 to 5.79) when compared with patients with complete resections without tumor rupture (relative risk = 1).

Patients With Complete Resections Without Tumor Rupture. The influence of extent of disease, tumor grade, and size were evaluated in the subset of patients who had complete resection of tumor without rupture ($n = 99$ patients evaluable). Within this population, only grade of tumor was significantly associated with overall survival ($p = 0.03$). Extent of disease ($p = 0.07$) and tumor size ($p = 0.1$) did not significantly influence survival. Thus, survivorship of patients with contiguous organ invasion (median, 36 months) or peritoneal implants (median, 36 months) were not significantly different when compared

TABLE 2. *Univariate Analysis of Factors That Influence Overall Survival*

Prognostic Factor	Evaluable Patients N (%)	Median Survival (mo)	p
Type of operation			<0.001*
Complete resection with no tumor rupture	99 (59)	48	
Incomplete resection	46 (28)	21	
Complete resection with tumor rupture	22 (13)	17	
Extent of disease			<0.001*
Localized	92 (53)	46	
Contiguous organ	21 (12)	36	
Implants resectable	19 (11)	28	
Implants unresectable	6 (3)	23	
Metastases	36 (21)	19	
Tumor grade			0.018*
Low	40 (39)	41	
High	62 (61)	36	
Tumor size (cm)			0.034*
<5	11 (8)	68	
5–10	45 (32)	32	
>10	86 (60)	27	
Site of primary lesion			NS
Age (yr)			NS
Sex			NS

* Factors entered into Cox proportional hazards model for regression analysis of joint effects and selection of significant prognostic factors.

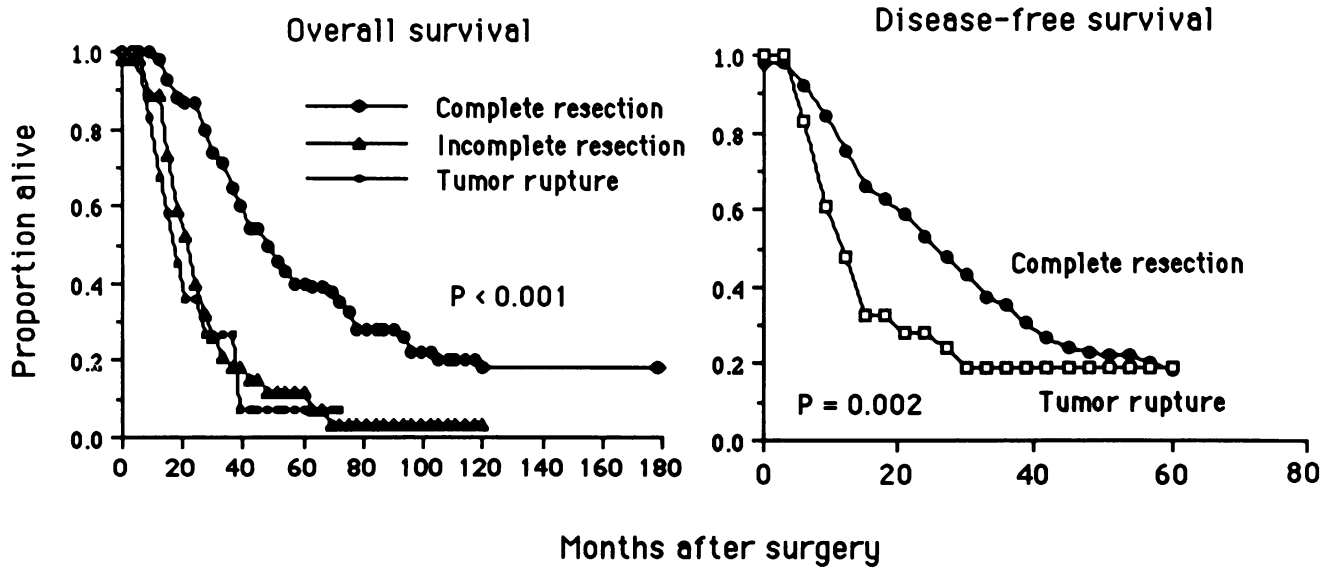

FIG. 2. Influence of type of operation on overall and disease-free survival rates. Complete resection without tumor rupture (n = 99); complete resection with tumor rupture (n = 22); incomplete resection (n = 46).

with patients with localized lesion (median, 46 months), provided that all primary tumor was removed without rupture.

Disease-free Survival

Univariate and Multivariate Analysis. Complete resections with and without tumor rupture were performed in 132 patients (69%) who were analyzed for factors influencing disease-free survival (Table 3). As of the last follow-up, only 10% of patients remained free of disease. The median interval to initial recurrence was 18 months (range, 3 to 232 months), and 60% of all recurrences occurred within 2 years of surgery (Fig. 1). Of the factors evaluated in a univariate analysis—tumor rupture (p = 0.002), extent of disease (p = 0.02), and tumor grade (p = 0.02)—were significantly related to disease-free survival. These three factors were each selected as significant factors in the multivariate analysis (Table 3). Tumor rupture had a dramatically adverse effect on disease-free sur-

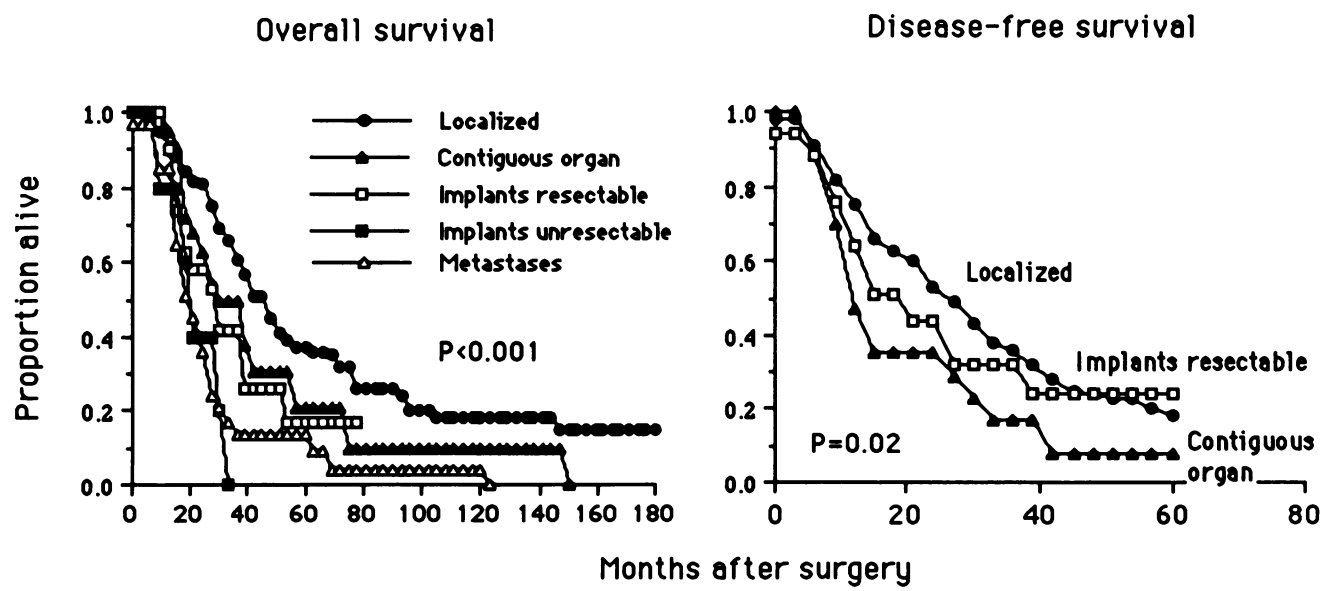

FIG. 3. Influence of extent of disease on overall and disease-free survival rates. Sample sizes for each category are shown in Table 2 for overall survival and Table 3 for disease-free survival.

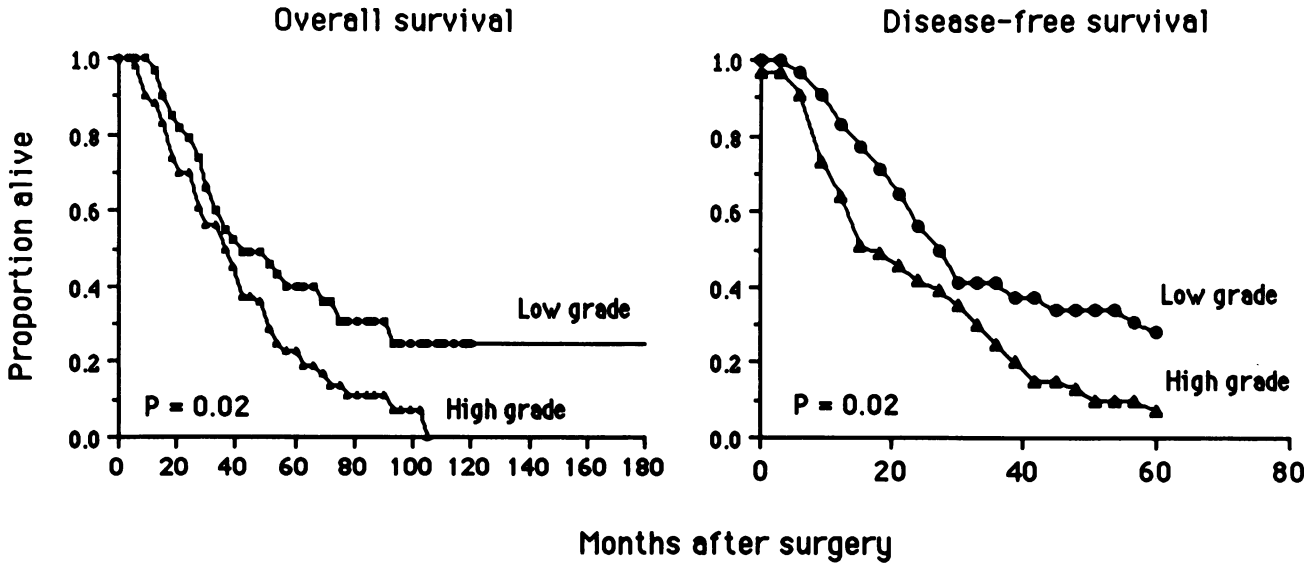

FIG. 4. Influence of tumor grade on overall and disease-free survival rates. Overall survival: low-grade (n = 40); high-grade (n = 61). Disease-free survival: low-grade (n = 36); high-grade (n = 45).

vival (median, 12 months) in comparison to patients without rupture (median, 26 months; Fig. 2). Patients with tumors that either invaded contiguous organs (median, 12 months; Fig. 3) or were high grade (median, 17 months; Fig. 4) experienced shorter disease-free survivals compared with localized (median, 27 months) or low-grade tumors (median, 27 months).

Analysis by Site of Tumor

An analysis of prognostic factors influencing overall survival was performed separately, based on the site of origin of the primary tumor: stomach (n = 72), small bowel (n = 79), and large bowel (n = 22; Table 4). Type of operation and the extent of disease were significantly related to overall survival in all primary sites analyzed. Tumor size was also significantly correlated with survival in stomach (p = 0.05) and large bowel (p = 0.04) tumors but not for small bowel tumors. Tumor grade showed significant trends only for tumors arising from the stomach (p = 0.07), but not for tumors arising from the small and large bowel.

The influence of the type of primary organ resection on overall survival and disease-free survival was evaluated

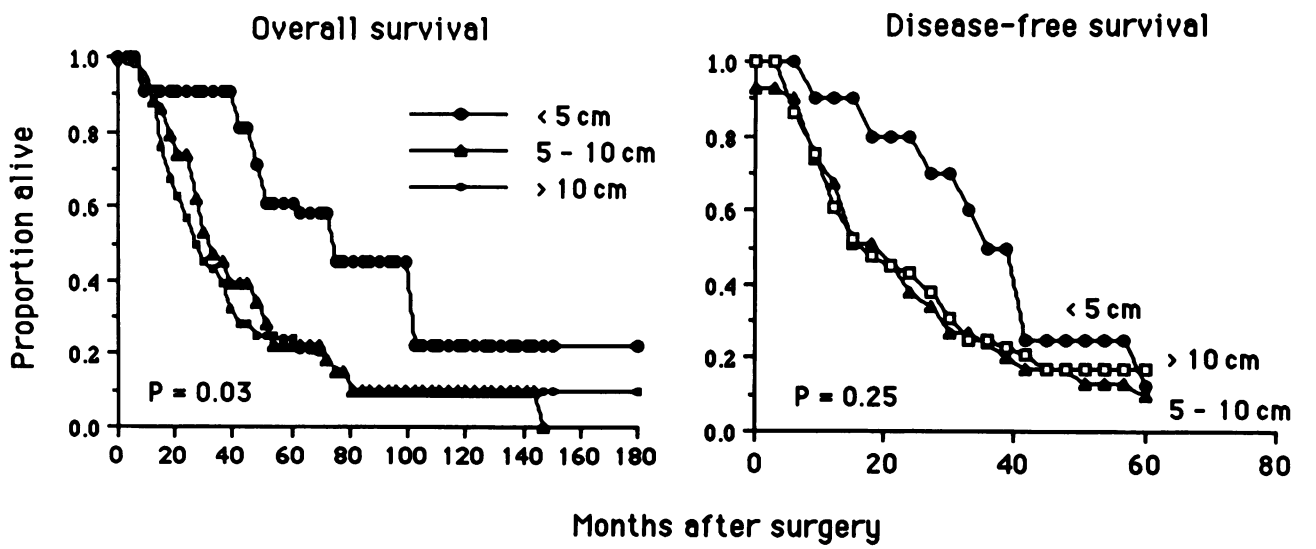

FIG. 5. Influence of tumor size on overall and disease-free survival rates. Sample sizes are shown in Table 2 for overall survival and Table 3 for disease-free survival.

TABLE 3. *Factors That Influence Disease-Free Survival After Complete Resection*

Prognostic Factor	Univariate analysis: Evaluable Patients N (%)	Univariate analysis: Median (mo)	Univariate analysis: p	Multivariate analysis*: Selected	Multivariate analysis*: Relative hazard†
Tumor rupture			0.002*	Yes	
No	99 (82)	26			
Yes	22 (28)	12			3.1
Extent of disease			0.02*‡	Yes	
Localized					
Implants	87 (73)	27			
resectable	17 (14)	19			
Contiguous organ	15 (13)	12			3.3
Tumor grade			0.02*	Yes	
Low	36 (44)	27			
High	45 (56)	17			1.9
Tumor size (cm)			NS		
<5	11 (10)	36			
5–10	31 (29)	19			
>10	66 (61)	17			
Site of primary lesion			NS		
Large bowel	16 (12)	39			
Stomach	45 (35)	25			
Small bowel	56 (43)	18			
Other	13 (10)	26			

* Prognostic factors entered into Cox model for regression analysis of joint effects and selection of significant prognostic factors ($p < 0.05$). Analysis was based on 72 patients with complete data.

† Relative risk of recurrence with reference to a value of 1 (no rupture, localized, and low-grade tumor).

‡ Localized *vs.* contiguous.

for tumors arising from the stomach and small bowel. The number of patients with large bowel tumors was too small for meaningful analysis. For appropriate comparisons, only localized tumors that were completely excised without tumor rupture were included. No differences were observed for wedge resections compared with more extensive surgery of the primary organ (gastrectomy or small bowel resection, Table 4). For stomach tumors, the median overall survival (67 months) and disease-free survival (33 months) after wedge resections were not statistically different after gastrectomy (median overall survival, 47 months; disease-free survival, 28 months; Fig. 6; $p = 0.26$). Similar results were observed when comparing for wedge resections against bowel resections for small bowel tumors (median overall survival, 75 *versus* 49 months; disease-free survival, 23 *versus* 26 months)

The impact of more radical locoregional surgery on outcome was also determined in the context of localized tumors. For tumors arising from the stomach, overall survival (median, 55 *versus* 41 months, $p = 0.65$, not significant [NS]) and disease-free survival (median, 33 *versus* 29 months, $p = 0.71$) were similar with or without resection of organs adjacent to the primary (Table 4 and Fig. 7). Similarly, no statistically significant differences were observed for small bowel tumors. Median overall survival and disease-free survival after resection of adjacent organs was 50 and 24 months, compared with 45 months ($p = 0.56$) and 26 months ($p = 0.7$) with surgery limited to the organ of origin, respectively.

Proposed Staging Classification

The ability of a staging classification incorporating prognostic factors of significance to stratify groups for overall and disease-free survival was examined. A TGM system was used for staging: T: T1, localized and <5 cm; T2, localized and ≥5 cm; T3, contiguous organ invasion or peritoneal implants; T4, tumor rupture. G: G1, low grade; G2, high grade. M: M0, no metastases; M1, metastases present. One hundred thirty-nine patients with complete data were evaluable for overall disease-free survival, and 93 patients were evaluable for disease-free survival. Plots of overall and disease-free survival curves for various combinations of the TGM system were generated: five composite stages that stratified patients in a stepwise fashion were identified. The corresponding TGM status and plots of overall survival for stages I through IVB are shown in Table 5 and Figure 8. Stages I (<5cm) and II (≥5cm) are localized lesions with low histologic grade. Stage III lesions are either high-grade tumors of any size or tumors with regional involvement (contiguous organ invasion or peritoneal implants). Stage IVA refers to patients with systemic metastases or unresectable tumor. Stage IVB is designated when tumor rupture has occurred despite resection of all macroscopic disease. Five-year overall survival rates for stages I, II, III, IVA, and IVB were 75%, 52%, 28%, 12%, and 7%, respectively. Disease-free survivals at 2 years were 89%, 57%, 47%, and 19% for stages I, II, III, and IVB, respectively.

TABLE 4. *Univariate Analysis of Factors That Influence Overall Survival for Each Site of Primary Tumor*

Prognostic Factor	Stomach			Small Bowel			Large Bowel		
	Evaluable Patients (n)	Median (mo)	p*	Evaluable Patients (n)	Median (mo)	p*	Evaluable Patients (n)	Median (mo)	p*
Type of operation			0.002			0.0001			0.007
Complete resections, no rupture	(44)	41		(44)	48		(14)	75	
Incomplete resections	(21)	16		(18)	24		(4)	24	
Complete resection, rupture	(5)	11		(12)	19		(2)	12	
Extent of disease			0.003			0.04			0.05
Localized	(35)	46		(45)	42		(10)	76	
Contiguous organ	(8)	29		(40)	40		(4)	36	
Implants resectable	(7)	15		(29)	29		(3)	14	
Implants unresectable	(2)	20		(4)	30		(0)	—	
Metastases	(17)	15		(13)	22		(4)	24	
Tumor size (cm)			0.05			0.9			0.04
<5	(4)	120+		(4)	45		(4)	104	
5–10	(14)	26		(21)	29		(5)	71	
>10	(38)	25		(35)	32		(9)	23	
Tumor grade			0.07			0.3			0.7
Low	(11)	56		(23)	39		(4)	71	
High	(29)	29		(21)	46		(10)	41	
Type of primary organ resection†			0.26			0.87			(—)‡
Wedge resection	(8)	67		(7)	75				
Bowel resection	(22)	47		(26)	49				
Adjacent organs resected†			0.65			0.56			(—)‡
None	(23)	55		(31)	50				
Yes	(7)	41		(3)	45				

* p value from comparison of survival by Lee-Desu statistic.
† Only localized tumors with complete resections without tumor rupture were compared.
‡ Variable not evaluated.

Discussion

Gastrointestinal leiomyosarcomas occur infrequently, accounting for only 0.1% to 3% of all gastrointestinal malignancies. Approximately 150 new cases are diagnosed annually in the United States.[6] Furthermore, a significant proportion of patients—90% in one series[7]—have their tumors discovered at operation without prior diagnosis

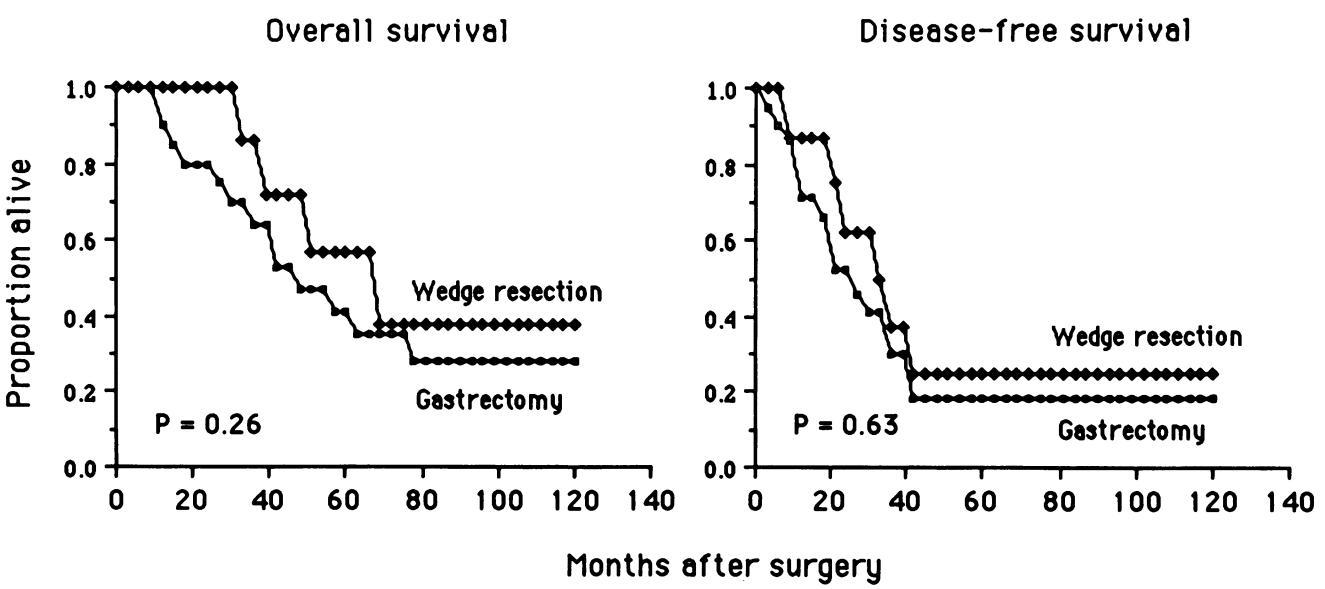

FIG. 6. Influence of wedge resection *vs.* gastrectomy for leiomyosarcomas localized to the stomach on overall and disease-free survival rates. Wedge resection (n = 8); gastrectomy (n = 22).

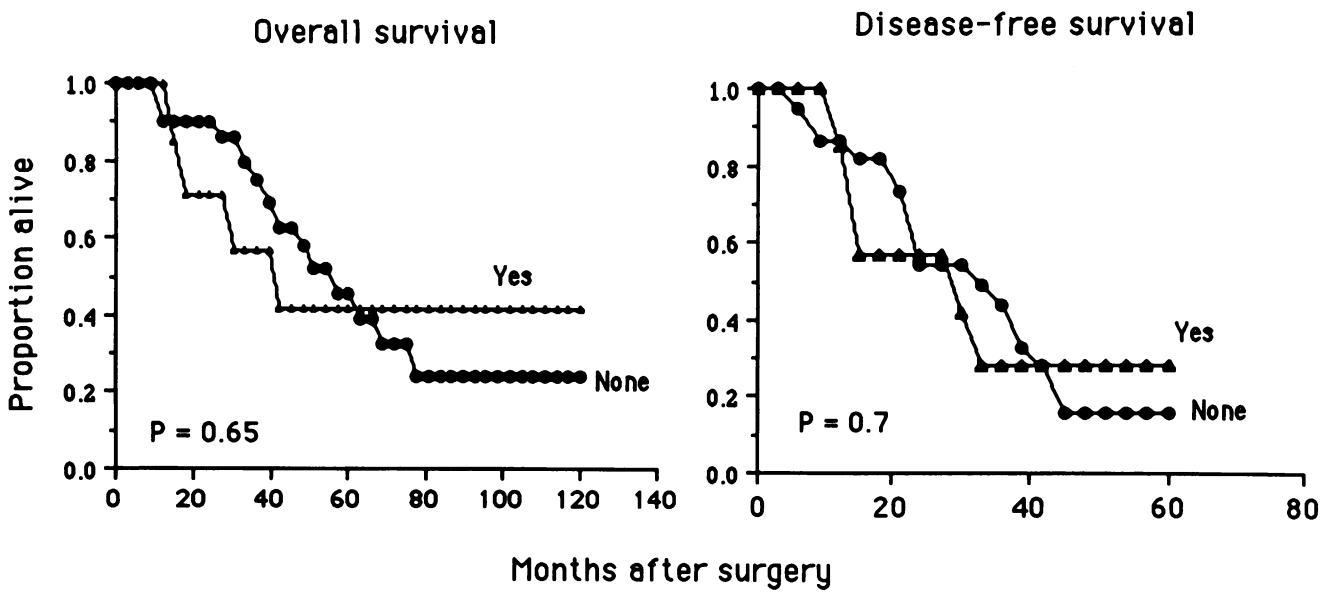

FIG. 7. Influence of resecting adjacent organs for localized leiomyosarcomas of the stomach on overall and disease-free survival rates. Resection (n = 7); no resection (n = 23).

when they present with bleeding, perforation, or obstruction. Thus, the surgeon is required to formulate adequate therapy, usually in an acute situation, for an exceedingly rare disease. Unfortunately, information regarding appropriate surgical management options and their corresponding outcomes remains scarce. The purpose of this study was to evaluate the influence of various clinicopathologic factors, including type of surgical resection, on overall and disease-free survival. From these results, the influence of surgically related procedures on outcome for both localized and invasive lesions could be clarified and appropriate therapeutic options formulated. Additionally, a staging classification incorporating significant prognostic factors was evolved. The ability of such a staging classification to stratify patients into prognostic groups for overall and disease-free survival was examined.

Overall survival at 5 years for patients with gastrointestinal leiomyosarcomas has been reported to be as high as 50%, whereas a considerable range (25% to 50%) exists from various series.[6] In this study, actuarial survival for all patients was only 28%. This finding is in agreement with Akwari et al.[8] and indicates that with adequate long-term follow-up, a high incidence of recurrences and subsequent fatalities can be anticipated. Only 10% of patients remained free of disease as of the last follow-up visit. The clinicopathologic features of this study cohort are comparable to those of other published series[9-14] and suggest that our sample population may be representative of the general population.

As has also been indicated by these reports,[9-15] variables such as tumor size, grade, completeness of tumor resection, and extent of the spread of disease are useful in pre-

TABLE 5. *Overall and Disease-Free Survival Based on M. D. Anderson Cancer Center Staging Classification for Gastrointestinal Leiomyosarcoma*

Stage	TGM	N (%)	Overall Survival (yr)			Disease-free Survival (yr)	
			5	8	10	2	4
I	T1 G1 M0	10 (7)	75%	56%	28%	89%	28%
II	T2 G1 M0	12 (9)	52%	28%	28%	57%	34%
III	T1-2 G2 M0 T3 any G M0	47 (34)	28%	14%	14%	47%	18%
IVA	M1 or residual disease after surgery	46 (33)	12%	4%	0%	—	—
IVB	T4	24 (17)	7%	—	—	19%	19%

Staging classification involving 139 patients for overall survival and 93 patients for disease-free survival.

T, tumor size and extra-organ involvement: T1 = localized; <5 cm; T2 = localized, ≥5 cm; T3 = contiguous organ invasion or peritoneal implants, any size; T4 = tumor ruptured, any size. G, tumor grade: G1 = low grade; G2 = high grade. M, distant metastases: M0 = no metastases; M1 = metastases present.

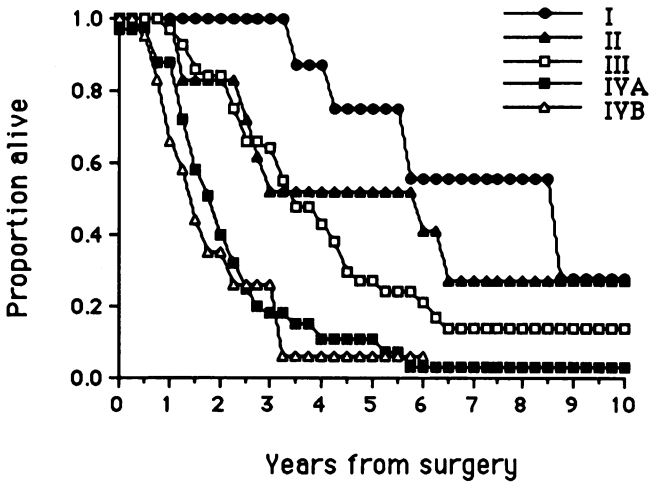

FIG. 8. Overall survival by staging of disease based on M. D. Anderson Staging Classification. Criteria and sample size for each stage are shown in Table 5.

dicting outcome of patients. Nevertheless, type of operation was identified as the only prognostic factor of significance via regression analysis in this study. Such findings underscore the central role of surgery in gastrointestinal leiomyosarcomas and emphasize that extirpative procedures with curative intent should be attempted for tumors invading adjacent organs or with associated peritoneal seeding. Removal of all gross disease improves outcome even in such patients with advanced disease. Thus, survival of patients with contiguous organ involvement or peritoneal implants was not significantly different compared with patients with localized lesions, provided all tumor was surgically excised. For *localized* lesions in the stomach or small bowel, wedge resection of the primary organ appears to be adequate, if all gross disease is removed. Wedge resections resulted in similar overall and disease-free survivals compared with gastrectomies or formal bowel resections. Similarly, resecting adjacent organs did not improve overall and disease-free survival. These results indicate that tumor spread either via mucosal extension or submucosal lymphatics is clinically less significant when compared with other routes of dissemination. This extrapolation is supported by the infrequent spread to regional lymph nodes (0% to 15%) from gastrointestinal sarcomas.[7,16,17] Thus, regional lymphadenectomy, as has been proposed by others,[16] would presumably not result in beneficial effects, particularly because the majority of patients present with systemic metastases as their first site of failure.[18]

Tumor rupture, either spontaneously or iatrogenically, was associated with an adverse influence on both overall and disease-free survival. Despite removal of all macroscopic tumor, affected patients are at extreme risk for early recurrences. A number of mechanisms may explain these observations. Tumors that are susceptible to rupture, presumably because of a large necrotic component, also may be inherently aggressive in their biologic behavior. Alternatively, the dissemination of tumor cells at the time of rupture, apart from seeding potential implants in the peritoneal cavity and the liver, also could lead to host immune suppression and result in an increase in tumor proliferative activity and appearance of recurrent disease. Although the mechanisms involved remain speculative, it is clear from the data that a grave prognosis can be anticipated in patients with gross spillage of tumor.

The grade of tumor has been shown to be of prognostic significance for survival.[8-15] In this study, tumors were not graded by an individual review and are therefore representative of the overall expertise of pathologists in a tertiary cancer center. As alluded to by Appelman,[19] the criteria for such grading are not rigidly defined; considerable subjectivity exists in their application. Morphologic criteria include cellularity, vascularity, amount of stroma, and number of mitotic figures, etc. Despite these limitations, grade of lesion was significantly related to disease-free survival and overall survival after complete resection of primary tumor. Patients with high-grade tumors, despite initial "curative surgery," are at higher risk for recurrences and are associated with a poor clinical outcome.

The analysis of prognostic factors based on tumors arising from different sites, as shown in Table 4, emphasizes the applicability of type of operation and extent of disease as important determinants irrespective of the primary site of origin. These results also support the feasibility of a staging classification suitable for all leiomyosarcomas arising from the gastrointestinal tract. The proposed staging classification may be useful in predicting prognosis and recommending adjuvant therapy for individual patients at high risk of relapse.

In conclusion, type of operation is the most important determinant of overall survival in patients with gastrointestinal leiomyosarcomas. Surgery remains the primary modality of treatment and extirpation of all macroscopic disease without gross spillage should be the goal of therapy. In patients with locally advanced disease, resection of peritoneal implants or contiguous organs invaded by the primary tumor should be attempted because survival is improved when complete resection of the primary tumor without rupture is performed. For localized lesions, removal of all macroscopic disease by wedge excision appears adequate because the addition of more extensive resection of either the primary organ or adjacent organs did not further increase survival. Despite such "curative surgery," the majority of patients will develop recurrent disease. Thus, the development of more effective multimodality adjuvant approaches is required to further improve survival for patients with gastrointestinal leiomyosarcomas.

Acknowledgments

The authors thank Anne Murphy for her outstanding assistance in data analysis.

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